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MS APPEAL BRIEF - PATENTS
0508-1105

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

In re application of

Filippo BELARDELLI et al. Conf. 1462

Application No. 09/845,042 Group 1644

Filed April 27, 2001 Examiner Gerald R Ewoldt

METHOD FOR GENERATING HIGHLY ACTIVE
HUMAN DENDRITIC CELLS FROM MONOCYTES

RESPONSE TO NOTIFICATION OF NON-COMPLIANT BRIEF

Assistant Commissioner for Patents
P.O. Box 1450
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February 9, 2007

Sir:

In response to the Notification of Non-Compliant Brief mailed January 9, 2007, a summary of the claimed subject matter may be found in the present specification as follows:

(v) Summary of the Claimed Subject Matter

The claimed invention is a method for producing dendritic cells from human mononuclear cells. As discussed in the present specification for example at page 1, lines 18-21, dendritic cells are recognized for their antigen-presenting capability, and thus play a key role in priming the immune

response. However, as discussed at page 3, lines 18-23 of the specification, the therapeutic use of dendritic cells has been limited by their low occurrence in peripheral blood and the difficulty of harvesting them from bone marrow and lymphoid tissue.

The invention improves upon techniques for producing dendritic cells from human mononuclear cells, e.g. peripheral blood monocytes. That is, previous researchers have shown that it is possible to make dendritic cells by culturing a patient's monocytes *ex vivo* under selected culturing conditions, which results in the transformation ("differentiation") of the cells into a distinct phenotype, namely that of immature dendritic cells (page 3, line 24 - page 4, line 24).

The present inventors have discovered that such dendritic cells can be made more rapidly and in a single step by differentiating the mononuclear cells in the presence granulyte/monocyte colony-stimulating factor (GM-CSF) and type I interferon gamma (IFN), for up to three days (page 5, line 9-14 and line 28-32). Independent claims 54, 63, 69 and 72 each reflect that discovery.

Claim 54 recites a process for deriving dendritic cells from mononuclear cells in culture wherein the mononuclear cells are peripheral blood mononuclear cells or CD14+ monocytes (page

16, lines 15-25), comprising culturing the mononuclear cells for a maximum of three days (page 9, lines 29 and 32-33) with type I IFN at a concentration of 400 to 10,000 IU/ml in the presence of GM-CSF at a range of 250-1,000 IU/ml (page 5, lines 33-34; page 6, lines 6-15; and page 26, lines 6-8), in the absence of IL-4 (page 26, lines 6-26), and collecting the cells within 3 days of culture (page 9, lines 29 and 32-33).

Claim 63 recites a method for the ex vivo derivation of dendritic cells from mononuclear cells within 3 days of culture, wherein said mononuclear cells are peripheral blood mononuclear cells (PBMC) or CD14+ monocytes (page 16, lines 15-25), comprising culturing type I IFN for a maximum of 3 days (page 9, lines 29 and 32-33) with said mononuclear cells from the beginning of said culture at a concentration range of 500 to 10,000 IU/ml, in the presence of GM-CSF at a concentration in a range of 500-1,000 IU/ml, and in the absence of IL-4 (page 26, lines 6-26).

In view of the above, it is apparent that claims 63 and 54 recite similar steps of culturing mononuclear cells. However, claim 63 recites different concentration levels of type I IFN and GM-CSF. The recited concentration levels for type I IFN and GM-CSF for all of the claims may be found in the specification at page 5, lines 33-34; page 6, lines 6-15; and page 26, lines 6-8.

Claim 69 recites a method for the ex vivo derivation of dendritic cells from mononuclear cells, wherein the mononuclear cells are isolated peripheral blood mononuclear cells (PBMC) or isolated CD14+ monocytes (page 16, lines 15-25), comprising culturing the isolated peripheral blood mononuclear cells (PBMC) or isolated CD14+ monocytes for a maximum of 3 days (page 9, lines 29 and 32-33) in a culture with type I IFN at a concentration 400-10,000 IU/ml and GM-CSF in a concentration of 250-1,000 IU/ml and in the absence of added IL-4 (page 26, lines 6-26), and collecting the cells within 3 days of culture.

Thus, claim 69 is similar to claim 63 but recites different concentration levels of type I IFN and GM-CSF. The recited concentration levels for type I IFN and GM-CSF for all of the claims may be found in the specification at page 5, lines 33-34; page 6, lines 6-15; and page 26, lines 6-8.

Claim 72 is a process for producing dendritic cells from mononuclear cells wherein the mononuclear cells are peripheral blood mononuclear cells (PBMC) or CD14+ monocytes (page 16, lines 15-25), comprising culturing the mononuclear cells for a maximum of 3 days (page 9, lines 29 and 32-33) with type I interferon (IFN) at a concentration in the range of 400-10,000 IU/ml in the presence of GM-CSF at a concentration in a range of 250-1,000 IU/ml, and wherein the dendritic cells

express higher levels of CD83 and CD25 antigens as compared to mononuclear cells or monocytes that have been cultured within 3 days of treatment with GM-CSF and IL-4.

Accordingly, claim 72 recites a similar process to that of claim 54 but further provides that the dendritic cells express higher levels of CD83 and CD25 antigens as compared to mononuclear cells or monocytes that have been cultured within 3 days of treatment with GM-CSF and IL-4 (pg. 19, lines 30-35).

In view of the concise explanation of the claimed subject matter set forth above, it is believed that the requirements of 37 CFR 41.37 (c)(1)(v) are satisfied. As a result, applicants respectfully request favorable consideration of the Appeal Brief filed on September 11, 2006.

Respectfully submitted,

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